



## Original Article

# Incidence and predictors of pericardial effusion as an early complication of catheter ablation for atrial fibrillation: The Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF)

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## ABSTRACT

**Background:** Pericardial effusion (PE) is one of the most frequent complications from catheter ablation of atrial fibrillation (AF). We assessed the prevalence and predictive factors of PE that require invasive treatment as an early complication of AF ablation.

**Methods:** The Japanese Heart Rhythm Society requested electrophysiology centers to register the relevant data of patients who underwent AF ablation during 6 months from 2011 to 2015. We compared the clinical profiles and the procedures of AF ablation between patients who had ablation-related PE and those who did not.

**Results:** Two-hundred-and-eight institutions reported the data of 8319 AF ablation sessions (age  $63.4 \pm 10.7$  years). A total of 414 complications occurred in 401 patients (4.8%). The incidence of invasively treated critical PE was 1.0% ( $n=85$ ) of total procedures, while conservatively treated noncritical PE appeared in 95 subjects. When clinical and procedural variables were compared between patients who suffered critical PE and 8140 PE-free patients, deep sedation ( $p=0.030$ ), impaired left ventricular function ( $p=0.031$ ), and periprocedural warfarin ( $p=0.023$ ) significantly increased the incidence of critical PE in univariate analysis. Use of 3-D imaging system ( $p < 0.001$ ) and a periprocedural direct oral anticoagulant (DOAC,  $p=0.002$ ) were related with lower incidence of critical PE. Among these factors, multivariate logistic regression analysis showed that 3-D imaging system (odds ratio 0.23 [95% CI: 0.14–0.39],  $p < 0.001$ ) and a periprocedural DOAC (odds ratio 0.49 [95% CI: 0.27–0.90],  $p=0.020$ ) are independent predictors of the lower incidence of PE.

**Conclusions:** Critical PE occurred in 1% of AF ablation procedures in Japan. Our results suggest that 3-D imaging system use independently reduces the frequency of PE. DOACs in the setting of catheter ablation of AF seemed to be non-inferior to warfarin in terms of safety and effectiveness.

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## 1. Introduction

To achieve efficacious and safe treatment of various arrhythmias, technological and technical innovations of catheter ablation are constantly being introduced into practice. To assess whether catheter ablation for the cure of atrial fibrillation (AF) is appropriately

performed in Japan, the Japanese Heart Rhythm Society (JHRS) started the annual nationwide registry of patients who underwent catheter ablation for AF: the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF) [1–4].

The acute complication rate has gradually decreased in recent years probably because of technological advances, improved techniques, and increased knowledge of procedural risks [5]. However, pericardial effusion (PE) is still one of the most frequent complications from AF ablation [6–9]. An earlier study has suggested that female sex and the number of procedures of each center are related with this complication [7,8]. The aim of this report is to evaluate the prevalence and predictive factors of PE as an early complication of AF ablation in Japan.

## 2. Material and Methods

The method of this survey has been previously reported [2,3]. In short, the survey was performed retrospectively using an online questionnaire. The JHRS members were notified by e-mail. Data on patient backgrounds, methods of pulmonary vein isolation and related techniques, complications, as well as the periprocedural pharmacological treatments were collected for AF ablation sessions performed in September 2011, May 2012, September 2012, September 2013, September 2014, and September 2015. Patient data included age, sex, previous AF ablation, AF type (paroxysmal [PAF]; persistent: or long-standing [LS] persistent), thromboembolism risk factors, and echocardiographic parameters. Centers with  $\geq 10$  procedures per month were defined as high-volume centers. PE was subdivided into two types, PE that needed drainage by pericardiocentesis or surgery (critical PE) and conservatively treated PE (noncritical PE).

Continuous variables with a normal distribution are expressed as mean  $\pm$  SD. First, comparison of clinical and procedural variables among three patient groups—critical PE, noncritical PE, and the remaining PE-free subjects (PE[-]) were performed by one-way analysis of variance with post hoc Bonferroni test. Categorical variables were compared using Tukey's test. Second, to elucidate the underlying factors of critical PE, variables were compared between the critical PE group and PE[-] patients. The data of noncritical patients with PE were intentionally excluded in the latter analysis because it is conceivable that underlying causes of noncritical PE are different from those of critical PE. Comparison of continuous variables between the two groups was done using unpaired Student's t-test. A multiple logistic regression analysis was performed for variables with univariate p value  $< 0.1$ , to detect the independent determinants for the occurrence of critical PE. A p  $< 0.05$  was considered statistically significant.

## 3. Results

### 3.1. General observations

Two-hundred-and-eight institutions reported the data of 8319 AF ablation sessions (mean age,  $63.4 \pm 10.7$  years; 73.8% male). In this population, there were 77.8% first AF ablation sessions (n=6471), 64.5% (n=5363) patients with PAF, 22.2% (n=1845) patients with persistent AF, and 13.4% (n=1111) patients with LS-persistent AF.

### 3.2. Complications

A total of 414 complications appeared in 401 patients (4.8%). Actual numbers of each event are shown in Table 1. PE occurred in 179 subjects, and approximately half of them required either

**Table 1**  
Summary of complications.

| No. of procedures         | 8319 | %    |
|---------------------------|------|------|
| Noncritical PE            | 94   | 1.1% |
| Critical PE               | 85   | 1.0% |
| Hematoma at puncture site | 81   | 1.0% |
| Sinus arrest              | 37   | 0.4% |
| Gastroparesis             | 19   | 0.2% |
| Phrenic nerve paralysis   | 21   | 0.3% |
| Pseudoaneurysm            | 15   | 0.2% |
| Cerebral infarction       | 6    | 0.1% |
| Air embolism              | 8    | 0.1% |
| Others                    | 48   | 0.6% |
| No. of events             | 414  | —    |
| No. of patients           | 401  | 4.8% |

Noncritical PE: conservatively treated pericardial effusion.

Critical PE: invasively treated pericardial effusion.

Abbreviation: PE, pericardial effusion.

cardiocentesis (n=83) or open-chest surgery (n=2). Thus, the incidences of critical PE and noncritical PE were 1.0% (n=85) and 1.1% (n=94) of the total procedures, respectively. Hematoma at the puncture site shared the second largest number of complications.

### 3.3. Comparison of clinical and procedural variables among three patient groups

Basic clinical profiles were compared among patients who suffered critical PE or noncritical PE and PE[-] patients (Table 2). PE tended to occur in older patients, but inter-group differences did not reach statistical significance. Noncritical PE appeared more frequently in the first AF ablation session (1<sup>st</sup> vs. redo, 82/6471 [1.3%] vs. 12/1848 [0.6%], p=0.027). History of a preceding ablation session did not significantly affect the incidence of critical PE (1<sup>st</sup> vs. redo, 71/6471 [1.1%] vs. 14/1848 [0.8%], p=0.200).

When procedural factors are compared among three patient groups (Table 3), 3-D imaging system and periprocedural direct oral anticoagulants (DOACs) were less frequently used in the critical PE group. Among 8319 patients, 2944 subjects (35.4%) were periprocedurally treated using warfarin, while 44.6% of them (n=3708) were given a DOAC (dabigatran 15.9%, rivaroxaban 13.3%, apixaban 14.3%, edoxaban 1.0%).

### 3.4. Results of multivariate logistic regression analysis on the incidence of critical PE

Comparing clinical and procedural variables between critical PE and PE[-] patient groups, five variables were found to have a

**Table 2**  
Comparison of clinical variables among three patient groups.

|                    | Critical PE     | Noncritical PE  | PE[-]           |
|--------------------|-----------------|-----------------|-----------------|
| Number of patients | 85 (1.0%)       | 94 (1.1%)       | 8140 (97.8%)    |
| Age (years)        | $65.0 \pm 10.1$ | $64.1 \pm 11.1$ | $63.4 \pm 10.7$ |
| Male               | 59 (69.4%)      | 60 (63.8%)      | 6019 (73.9%)    |
| First session      | 71 (83.5%)      | 82 (87.2%)*     | 6318 (77.6%)    |
| PAF                | 55 (64.7%)      | 60 (63.8%)      | 5248 (64.5%)    |
| Lone AF            | 23 (27.1%)      | 19 (20.2%)      | 1862 (22.9%)    |
| Hemodialysis       | 1 (1.2%)        | 2 (2.1%)        | 94 (1.2%)       |
| CHA2DS2-VASc score | $2.06 \pm 1.61$ | $2.07 \pm 1.65$ | $1.88 \pm 1.43$ |
| LVEF (%)           | $65.2 \pm 7.2$  | $64.4 \pm 9.1$  | $63.5 \pm 9.8$  |
| LAD (mm)           | $39.4 \pm 6.6$  | $41.3 \pm 7.9$  | $40.4 \pm 6.9$  |

Data are presented as n (%) or mean  $\pm$  SD.

Abbreviations: AF, atrial fibrillation; LAD, left atrial diameter; LVEF, left ventricular ejection fraction; PAF, paroxysmal AF; PE, pericardial effusion.

\* p  $< 0.05$  vs. PE[-].

**Table 3**  
Comparison of procedural factors among three patient groups.

|                         | Critical PE  | Noncritical PE | PE[-]        |
|-------------------------|--------------|----------------|--------------|
| Number of patients      | 85 (1.0%)    | 94 (1.1%)      | 8140 (97.8%) |
| 3-D imaging system      | 65 (76.5%)*  | 92 (97.9%)     | 7661 (94.2%) |
| Cryoballoon             | 4 (4.7%)     | 1 (1.1%)       | 322 (4.0%)   |
| CFAE ablation           | 11 (12.9%)   | 10 (10.6%)     | 880 (10.8%)  |
| LA linear ablation      | 15 (17.6%)   | 24 (25.5%)     | 1956 (24.0%) |
| Deep sedation           | 50 (53.8%)   | 51 (54.3%)     | 3831 (47.1%) |
| Periprocedural Warfarin | 40 (47.1%)   | 39 (41.5%)     | 2865 (35.2%) |
| Periprocedural DOAC     | 24 (28.2%)** | 36 (38.3%)     | 3648 (44.8%) |
| High volume center      | 53 (62.4%)   | 69 (73.4%)     | 5316 (65.3%) |

Abbreviations: CFAE, complex fractionated atrial electrogram, DOAC, direct oral anticoagulant; LA, left atrial; PE, pericardial effusion.

\*  $p < 0.01$  vs. critical PE and PE[-].

\*\*  $p < 0.01$  vs PE[-].

**Table 4**  
Results of univariate analysis and multiple logistic regression analysis between critical PE and PE[-].

|                    | Univariate p-value | Odds ratio (95% CI) | multivariate p-value |
|--------------------|--------------------|---------------------|----------------------|
| LVEF               | 0.031              | 1.02 (1.00–1.05)    | 0.096                |
| 3-D imaging system | < 0.001            | 0.23 (0.14–0.39)    | < 0.001              |
| Deep sedation      | 0.031              | 1.50 (0.96–2.33)    | 0.073                |
| Warfarin           | 0.023              | 0.97 (0.56–1.68)    | 0.911                |
| DOAC               | 0.002              | 0.49 (0.27–0.90)    | 0.020                |

Values of each variable are provided in Table 2 and Table 3.

Abbreviations: CI, confidence interval; DOAC, direct oral anticoagulant; LVEF, left ventricular ejection fraction; PE, pericardial effusion.

possible association with critical PE ( $p$  value < 0.1). As shown in Table 4, the 3-D imaging system was used in 94.2% of patients in the PE[-] group. In contrast, it was less frequently used in subjects who suffered critical PE (76.5%, odds ratio 0.23 [95% confidence interval (CI): 0.14–0.39],  $p < 0.001$ ). Periprocedural DOAC was more frequently used in PE[-] patients than patients with vertical PE (44.8% vs. 28.2%, odds ratio 0.49 [95% CI: 0.27–0.90],  $p = 0.020$ ). Neither left ventricular ejection fraction, deep sedation, or periprocedural warfarin was significantly related with critical PE.

## 4. Discussion

### 4.1. Major findings

The major findings of the present study are: 1) PE that needed invasive treatment, i.e., critical PE, occurred in 1.0% of AF ablation cases; 2) 3-D imaging system use and periprocedural use of a DOAC were related with lower incidence of critical PE.

### 4.2. Earlier studies

Deshmukh et al. analyzed overall complications associated with AF ablation in the United States [9]. In 93,801 procedures performed between 2000 and 2010, they found that the frequency of complications was 6.29% with cardiac complications being the most frequent (2.54%). There was a significant association between hospital volume and adverse outcomes. Also, catheter ablation of AF in older patients or in female subjects was associated with a

higher total complication rate in comparison with younger age subjects or male patients.

The results of a worldwide survey on the incidence of cardiac tamponade after catheter ablation of AF was reported by Michowitz et al. [8]. In 34,943 procedures (men 72%), cardiac tamponade occurred in 289 cases (0.9%). They also noticed that the number of procedures in each hospital and female sex were related with this complication.

### 4.3. Interpretation of the present results

The frequency of critical PE in our registry (1.0%) was comparable with those of earlier studies (1.2% [6], 1.3% [7], and 0.9% [8]). Results of multiple logistic regression analysis showed that only two factors, the use of a 3-D imaging system and periprocedural DOAC, were significantly associated with the occurrence of PE. Although the use of 3-D imaging systems, CARTO system in most cases, may reduce the procedure time and warrant precise identification of the foci and mechanisms of arrhythmic substrates, our observation suggests that they also enhance the safety of AF ablation.

In earlier studies, uninterrupted warfarin was superior to an interrupted oral anticoagulant strategy for the outcome of AF ablation [10–12]. DOACs have been shown to be comparatively useful as warfarin as a periprocedural oral anticoagulant [4,13–16]. In the present survey, the rate of warfarin use increased in the sequential order from PE[-] to critical PE, noncritical PE being intermediate, while the rate of DOAC use decreased in the same order. Thus, periprocedural warfarin and DOAC seemed to have affected the occurrence of PE in the opposite direction. However, results of multiple logistic regression analysis that assessed the determinants of critical PE suggest that DOACs may serve to avoid critical PE, and that periprocedural warfarin does not have either a favorable or an unfavorable effect on the incidence of critical PE.

There exist several possible explanations for this observation, such as the differences in the temporal profile of anticoagulant status during the periprocedural period of ablation or in the regimen of heparin. A recent meta-analysis [17] reached a similar view to ours in that periprocedural use of a DOAC is as effective as warfarin for the prevention of thromboembolic events and may contribute to reduce the incidence of bleeding complications. More information is necessary to confirm the merit of DOACs for averting critical PE.

Contrary to observations in earlier studies [8,9], we failed to detect an appreciable impact of female sex, age, or center volume on the frequency of PE. One possible explanation is that physicians tend to pay more careful attention to older or female patients before and during AF ablation. However, true reasons of these discrepancies between earlier studies and ours are not clear.

### 4.4. Limitations

The risk of early complications is under the influence of many factors, such as clinical background of patients and the techniques of AF ablation [2]. It is possible that the present results did not adequately point out the most momentous factor related to PE. Special care should be taken to interpret the present results that might have been biased by the limitations inherent to observational studies.

DOACs were collectively analyzed. Also, details of heparin use and duration of interruption of an oral anticoagulant were not included in the analysis. Therefore, the merit of each DOAC, if it exists, to reduce the risk of PE or other bleeding complications is unknown.

## 5. Conclusions

Critical PE occurred in 1% of subjects who underwent catheter ablation of AF in Japan. The present results suggest that the use of a 3-D imaging system and periprocedural DOAC may decrease the incidence of PE.

## Conflict of interest

All authors declare no conflict of interest related to this study.

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## References

- [1] Murakawa Y, Nogami A, Shoda M, et al. Nationwide survey of catheter ablation for atrial fibrillation: The Japanese catheter ablation registry of atrial fibrillation (J-CARAF)—A report on periprocedural oral anticoagulants. *J Arrhythm* 2015;31:29–32.
- [2] Inoue K, Murakawa Y, Nogami A, et al. Clinical and procedural predictors of early complications of ablation for atrial fibrillation: analysis of the national registry data. *Heart Rhythm* 2014;11:2247–53.
- [3] Murakawa Y, Nogami A, Shoda M, et al. Nationwide survey of catheter ablation for atrial fibrillation: the Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF)—report of 1-year follow-up. *Circ J* 2014;78:1091–6.
- [4] Murakawa Y, Nogami A, Shoda M, et al. Report of periprocedural oral anticoagulants in catheter ablation for atrial fibrillation: The Japanese Catheter Ablation Registry of Atrial Fibrillation (J-CARAF). *J Arrhythmia* 2016. <http://dx.doi.org/10.1016/j.joa.2016.10.002>.
- [5] Gupta A, Perera T, Ganesan A, et al. Complications of catheter ablation of atrial fibrillation: a systematic review. *Circ Arrhythm Electrophysiol* 2013;6:1082–8.
- [6] Spragg DD, Dalal D, Cheema A, et al. Complications of catheter ablation for atrial fibrillation: incidence and predictors. *J Cardiovasc Electrophysiol* 2008;19:627–31.
- [7] Dagues N, Hindricks G, Kottkamp H, et al. Complications of atrial fibrillation ablation in a high-volume center in 1,000 procedures: still cause for concern? *J Cardiovasc Electrophysiol* 2009;20:1014–9.
- [8] Michowitz Y, Rahkovich M, Oral H, et al. Effects of sex on the incidence of cardiac tamponade after catheter ablation of atrial fibrillation: results from a worldwide survey in 34 943 atrial fibrillation ablation procedures. *Circ Arrhythm Electrophysiol* 2014;7:274–80.
- [9] Deshmukh A, Patel NJ, Pant S, et al. In-hospital complications associated with catheter ablation of atrial fibrillation in the United States between 2000 and 2010: analysis of 93 801 procedures. *Circulation*. 2013;128:2104–12.
- [10] Santangeli P, Di Biase L, Horton R, et al. Ablation of atrial fibrillation under therapeutic warfarin reduces periprocedural complications: evidence from a meta-analysis. *Circ Arrhythm Electrophysiol* 2012;5:302–11.
- [11] Di Biase L, Burkhardt JD, Mohanty P, et al. Periprocedural stroke and management of major bleeding complications in patients undergoing catheter ablation of atrial fibrillation: the impact of periprocedural therapeutic international normalized ratio. *Circulation* 2010;121:2550–6.
- [12] Hakalahti A, Uusimaa P, Ylitalo K, et al. Catheter ablation of atrial fibrillation in patients with therapeutic oral anticoagulation treatment. *Europace* 2011;13:640–5.
- [13] Kim JS, She F, Jongnarangsin K, et al. Dabigatran vs. warfarin for radiofrequency catheter ablation of atrial fibrillation. *Heart Rhythm* 2013;10:483–9.
- [14] Lakkireddy D, Reddy YM, Di Biase L, et al. Feasibility & Safety of Uninterrupted Rivaroxaban for Periprocedural Anticoagulation in Patients Undergoing Radiofrequency Ablation for Atrial Fibrillation: Results from a Multicenter Prospective Registry. *J Am Coll Cardiol* 2014;63:982–8.
- [15] Lakkireddy D, Reddy YM, Di Biase L, et al. Feasibility and safety of dabigatran versus warfarin for periprocedural anticoagulation in patients undergoing radiofrequency ablation for atrial fibrillation: results from a multicenter prospective registry. *J Am Coll Cardiol* 2012;59:1168–74.
- [16] Rillig A, Lin T, Plesman J, et al. Apixaban, Rivaroxaban, and Dabigatran in Patients Undergoing Atrial Fibrillation Ablation. *J Cardiovasc Electrophysiol* 2016;27:147–53.
- [17] Zhao Y, Yang Y, Tang X, et al. New oral anticoagulants compared to warfarin for perioperative anticoagulation in patients undergoing atrial fibrillation catheter ablation: a meta-analysis of continuous or interrupted new oral anticoagulants during ablation compared to interrupted or continuous warfarin. *J Interv Card Electrophysiol* 2017 Jan 12. <http://dx.doi.org/10.1007/s10840-016-0221-7>.